

### **REMARKS**

The present response is being submitted in reply to the Final Office action issued on March 27, 2008. The Applicants wish to thank the Examiner for the withdrawal of the previous rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112. Claims 31-52 are pending in this application, each of which is now rejected. Reconsideration is respectfully requested in light of the following remarks.

#### **Rejection of claims 31-52 under 35 U.S.C. 103(a)**

Claims 31-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yadav, et al. (*Microwave-assisted Rapid Synthesis of the Cytotoxic Alkaloid Luotonin A*), Tetrahedron Letters, Vol. 43, 1905-07 (2002) for the reasons set forth in the Office action dated August 23, 2007. The Examiner essentially maintains the position that Yadav, et al. teach the limitations of the presently claimed invention, but do not teach an explicit motivation for a skilled artisan to modify the molar ratios of the two reactants relative to one another. Therefore, the Examiner concludes that the invention as presently claimed would be obvious because "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." In this instance, the Examiner states that it would have been obvious to one having ordinary skill in the art to increase the reactants and expect such addition to drive the chemical reaction to the right, and thereby increase the products. Moreover, the Examiner has concluded that changing the molar ratio of the reactants of Yadav, et al. is an obvious modification of Yadav, et al. to one skilled in the art in order to arrive at the present invention.

The Examiner also states in the Office action that the limitation of the presently

claimed invention of heating the reaction mixture to two separate temperatures for two separate periods of time is not a critical limitation of the present invention over the prior art. Therefore, in the Examiner's opinion, the slight modification of the process of Yadav, et al. does not optimize the production method and thus does not seem to impart patentability because the temperature modifications are within the purview of one skilled in the art.

The Applicants respectfully disagree with the Examiner's position and submit that to establish a *prima facie* case of obviousness, three basic criteria must be met, as set forth in M.P.E.P. § 2142. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

As the Examiner is aware, Yadav, et al. teach a process for producing microwave-assisted synthesis of luotonin A or quinazolines, wherein cyclocondensation of lactams with isatoic anhydride proceeds rapidly in high yields with high selectivity under microwave irradiation under solvent-free conditions. The advantages of the microwave-assisted reaction include that conventional heating at 120°C and longer reaction times required for the condensation of lactams with isatoic anhydride are totally avoided (page 1906, right column, 2<sup>nd</sup> paragraph). Yadav, et al. even presume that their method is becoming an alternative and substitute heating source. When comparing the microwave-assisted synthesis of Yadav, et al. with a conventional method of synthesis, Yadav, et al. teach that some quinazolines were obtained by a reaction in an oil bath at 120°C for 5 to 8

hours, but with moderate yields of 60 to 75%.

Regarding present claims 31-39, the Examiner states in the Final Office action that Yadav, et al. do not teach (i) to use a ratio of the two reactants other than an equimolar ratio, and (ii) to utilize a two-stage heating process wherein the first temperature is maintained for a period of time before maintaining a second temperature for a second period of time.

With respect to the difference that Yadav, et al. teach the use of equimolar amounts whereas the present claimed process according to claim 31 utilizes a 1.5 to 5 molar excess of 2-pyrrolidone, the Examiner states that it was obvious at the time the present invention was made to increase the amount of one reactant to drive the chemical reaction for increasing the yield of products, as discussed above. In this regard, the Applicants refer to Example 2 of the present specification. In contrast to the Examiner's position, the Applicants respectfully submit that the present specification at Example 2 supports the finding that a molar ratio of 2-pyrrolidone to isatoic acid anhydride of 3:1 yielded less product than a molar ratio of 2.2:1. It is thus submitted that this observation clearly is in contrast to the Examiner's position, and further supports the non-obviousness of the presently claimed invention.

Furthermore, the Applicants submit that the first temperature of the process as claimed in claim 31 may be the temperature employed by Yadav, et al. However, the second temperature is clearly above the temperature which is taught by Yadav, et al. In particular, Yadav, et al. fail to teach or provide any suggestion that the temperature of the reaction may be increased beyond 120°C, which is the highest observed temperature

during microwave irradiation. It is submitted that the entire disclosure of Yadav, et al. would refrain one skilled in the art to attempt to increase the yield by increasing the temperature above 120°C instead of using microwave irradiation. Therefore, the Applicants submit that Yadav, et al. do not render the presently claimed process obvious to one skilled in the art at the time the present invention was made since every limitation is not disclosed.

Regarding claims 40 – 52, it is submitted that the process of claim 40 is based on the process of claim 31, but recites the further process steps subsequent to the production of a compound of formula (I), i.e., the steps of performing a reduction reaction such that compound (I) is converted to compound (III) and liberating compound (III) from the salt. Therefore, for the reasons set forth above, the prior art fails to render claim 40 and the respective dependent claims as being obvious.

The Applicants further submit that Yadav, et al. may teach processes to obtain quinazolines from performing cyclocondensation of lactams with isatoic anhydride. However, Yadav, et al. do not teach any further processing of the product directly obtained by the cyclocondensation. Therefore, Yadav, et al. clearly fail to provide any disclosure that would motivate one skilled in the art to further process the product obtained by cyclocondensation to get compound (III) of the present invention. In the absence of any prior art disclosure with respect to the production of compound (III) or a similar compound, the Applicants submit that there is no reason that a person of ordinary skill in the art would have good reason to pursue known options within his or her technical grasp in order to further process compound (I) for arriving at compound (III) as

alleged by the Examiner.

It is therefore respectfully submitted that the present invention defined in the present claims is patentably distinguishable over the prior art teachings under 35 U.S.C. 103(a). Based on the aforementioned differences between the presently claimed invention and the prior art, each and every element of the present invention recited in the present claims are not set forth in the Yadav, et al. Moreover, one skilled in the art would not be motivated to modify Yadav, et al. to arrive at the presently claimed invention. Even if one were to do so, there would be no expectation of success. Therefore, the Applicant respectfully requests that this rejection be withdrawn.

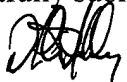
#### Conclusion

For the foregoing reasons, it is believed that the present application, as amended, is in condition for allowance, and such action is earnestly solicited. Based on the foregoing arguments and the deficiencies of the prior art reference, the Applicants strongly urge that the obviousness-type rejection be withdrawn. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

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Respectfully submitted,

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